1042-84 Elevated Plasma Level of Placental Growth Factor Is Correlated With Peripheral Monocyte Fraction in Patients With Acute Myocardial Infarction

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Background: Earlier studies have revealed that bone mallow derived stem cells (BMSM) participate in wound healing and regeneration of infarct tissue in acute myocardial infarction (AMI). However, it remains unknown how infarct heart tissue stimulates and recruits BMSC to the heart. Placental growth factor (PlGF), a member of vascular endothelial growth factor (VEGF) family, exerts its angiogenic property through binding to VEGF receptor-1. Furthermore, PlGF has been reported to induce BMSC peripheral mobilization. In this study, we studied the serial changes of plasma PlGF levels and white blood cell profile after AMI in human, and also studied the tissue expression of PlGF in the infarct myocardium of mouse AMI model. **Method and results:** Thirty five AMI patients AMI (67.5 y/o) were enrolled, and plasma cytokine levels were measure by ELISA. The plasma PlGF levels of AMI patients significantly increased compared to those in age-matched controls (36.8+/-31.9, 13.3+/-5.2 pg/ml, p<0.0001). Monocyte fraction was elevated in AMI peripheral blood from 3rd to 7th day of AMI, and PlGF positively correlated to peak monocyte fraction (r= 0.496, p<0.005), while PlGF did not correlate to polymorphic neutrophil fraction. Plasma levels of VEGF and stem cell factor also elevated in AMI than control, but they did not correlate to monocyte fraction. In the AMI mouse model, quantitative real time PCR revealed that PlGF mRNA expression was significantly (26.6 +/-5.2 times, p<0.001) increased in infarct heart compared with sham operated heart on 3rd surgical day. Furthermore, immunohistochemical staining showed that PlGF protein was overexpressed mainly in vascular tissue in infarct region, but scarcely in non-infarct region. Vascular expression of PlGF protein was not detected in sham-operated heart. **Conclusion:** The present study demonstrates that plasma PlGF levels are increased in AMI patients, and correlated with cell number of monocyte fraction, and PlGF mRNA and protein are over-expressed in vascular tissue at the site of infarct myocardium. Elevated plasma PlGF might have effect on the recruitment of monocyte, as well as vascular progenitor cells, from bone marrow to peripheral circulation.

1042-85 Tumor Necrosis Factor-α Blockade: A Key Inhibition to Modulate the Inflammatory Response in Patients With Unstable Angina?

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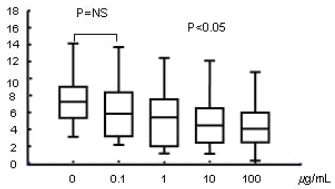
Background: Tumor necrosis factor-α (TNF-α) is a pro-inflammatory cytokine increased in unstable angina (UA). TNF-α activates NF-kB and favours the expansion of $CD4^+CD28^{null}$ T-cells, an aggressive and rare pro-inflammatory lymphocyte subset, frequently observed in UA. We used Infliximab, a monoclonal antibody against TNF-α , to modulate in vitro the inflammatory response in patients with UA.
Methods: Peripheral blood samples were collected from 17 patients with UA (Braunwald's class IIIB). The monocyte production of TNF-α was assessed after 4 hours incubation with lipopolysaccharide (LPS 1ng/mL) and after incubation with LPS (1ng/m) plus Infliximab (0.1, 1, 10 and 100 μg/mL). TNF-α levels were measured by ELISA. The modulation of $CD4^+CD28^{null}$ T- cell frequency by Infliximab was assessed with flow cytometry after 24 hours incubation of whole blood with and without Infliximab (0.1, 1, 10 and 100 μ g/mL).
Results: TNF-α production significantly increased after incubation with LPS (median) (from 0 to 266.3 pg/ml, P=0.03) but was reduced to 0.43 pg/ml by 0.1 μ g/mL of Infliximab (P=0.001) and totally inhibited by higher doses . $CD4^+CD28^{null}$ T-cell frequency was reduced from 6.2% to 4.9%, 4.5% and 4.1% after incubation with 1, 10, and 100 μ g/mL of Infliximab, respectively (see figure; P<0.05 by ANOVA).
Conclusion: In UA, monocyte production of TNF-α and the frequency of $CD4^+CD28^{null}$ T-cells are reduced by Infliximab. These results may introduce novel anti-inflammatory strategies for the treatment of UA.



Frequency (%) of $CD4^+CD28^{null}$ T-cells after incubation with increasing doses of Infliximab

1042-86 Risk Stratification in ST-Segment Elevation Myocardial Infarction With Multiple Biomarkers

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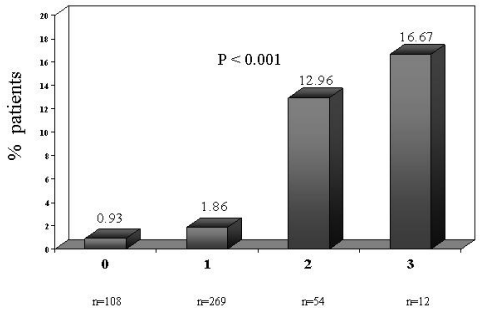
***Background*:** Among patients with STEMI, cardiac troponin, B-type natriuretic peptide and C-reactive protein independently predict adverse cardiac events. However, their utility in combination remains untested. We hypothesize that in patients with STEMI undergoing fibrinolysis, simultaneous assessment of BNP, CRP and troponin I on admission provides useful complementary information with respect to short-term mortality.
Methods: In ENTIRE-TIMI 23 trial, 483 patients with STEMI <6 hours from symptom onset were treated with either TNK or combination of half-dose TNK plus abciximab, and with either unfractionated heparin or enoxaparin. We evaluated the relationship between the number of elevated biomarkers and mortality at 30 days among 443 patients, in whom samples for measurement of all three biomarkers were available.
Results: Mortality by 30 days increased in proportion to the number of elevated biomarkers, revealing an 18-fold gradient between those with 3 versus none of the biomarkers elevated (P<0.001) (Fig). There was a trend towards more new CHF by 30 days in patients with more elevated biomarkers (P=0.14). Number of patients with either death or CHF by 30 days was also directly proportional to the number of elevated biomarkers (P<0.001).
Conclusion: Among patients with STEMI, a multimarker approach combining CRP, BNP and TnI provides incremental information regarding short-term mortality risk. Such an approach may prove useful for enhancing clinical decision-making in this population.

30-day mortality in ENTIRE-TIMI 23



1042-87 White Blood Cell Count Predicts Angiographic Findings in Patients With Acute Coronary Syndromes

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Elevation of inflammatory markers has been associated with adverse outcome in patients with acute coronary syndromes. We sought to assess the relation between baseline white blood cells (WBC) count and angiographic findings and outcome in patients with non-ST elevation acute coronary syndromes.
Methods: We evaluated the relation between baseline WBC count, angiographic findings and outcome in 590 patients in a cohort of 1293 consecutive patients with acute coronary syndromes. Angiograms were read by two independent readers blinded to patient data. We grouped the WBC count into low (<25^{th} percentile), intermediate (25^{th}-75^{th} percentile) and high (>75^{th} percentile).
Results: Baseline WBC count ranged from 3530 to 35800, and the median was 9300 (25^{th}-75^{th} 7700-11500). Patients with high WBC count were older, more likely to be male and had more frequently history of hypertension and diabetes. Angiographic findings are shown in the table. Higher WBC counts were associated with higher rates of angiographically thrombus, complicated plaque and extent of coronary artery disease. Likewise, patients with high WBC count has 2 fold increase risk of death or myocardial infarction at 180 days compared with patients with low or intermediate WBC count (14.2% versus 7.5%, p=0.026).
Conclusions: In this study, elevation of white blood cells count was associated with more extensive CAD, more complex coronary lesions and higher occurrence of death / myocardial infarction at 180 days.

Angiographic findings

	Low WBC Count n=146	Intermediate WBC n=293	High WBC Count n=141	p
Complicated Plaque	36.3%	46.4%	51.1%	0.033
Thrombus present	11.0%	19.1%	23.4%	0.019
3-Vessels Disease	17.8%	25.0%	29.3%	0.070